REMARKS

The Office Action mailed May 20, 2005, has been carefully reviewed.

Claims 35, 36 and 42, have been canceled, and claims 33, 45 and 47 have been amended.

Claims 24 – 32 stand withdrawn as deemed to be allegedly directed to a non-elected invention.

Claims 33- 40 and 43-48 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent Publication 2004/0091500.

Claims 35 – 37 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

Claim 45 also stand objected to for lack of antecedent basis in the specification for a claimed limitation.

The claims as amended herein are fully supported by the application as originally filed. No new matter has been added. Reconsideration and allowance of the present application are respectfully requested in view of the foregoing amendments and the following additional remarks which have addressed all the grounds for objection or rejection or otherwise have rendered them moot.

Response to Objections

Claims 41 and 42 were objected to as being exact duplicates. Claim 42 has been accordingly canceled and this objection is now moot.

Claim 45 was objected to for reciting a limitation of at least 100 µg, said limitation not found in the specification. Applicants appreciate the Examiner notifying them of the apparent typographical error. Claim 45 has been amended to recite at least 10 µg. Support for this can

be found in the last paragraph of page 3 of the specification. Accordingly, this objection should also be withdrawn.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claims 35 – 37 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. According to the Examiner, the newly added claim language drawn to 10% or 5% or elimination of IgE binding has no support in the originally filed specification or claims. Applicants respectfully disagree with the Examiner and hereby traverse as follows.

The Examiner's attention is drawn to paragraph 4, page 4 of the specification where the Applicants explicitly stated:

> Preferably the allergenic activity of the derivative is less than 50% of the allergenic activity of the respective wild type protein from which it is derived. More preferably the allergenic activity of the derivatives is less than 25% of the wild type protein. In the most preferred embodiment the derivative has substantially no allergenic activity.

Further, the Applicants in paragraphs 2 and 4 defined what they mean by allergenic activity and how it is to be determined. Moreover claim 33, from which claims 35 – 37 depend recite allergenic activity of 50% or less. The phrase, "50% or less", encompasses 50% or less allergenic activity and upon allowance, grants the Applicants the right to exclude others from exploiting the subject matter of claim 33, wherein the allergenic activity is 50% or less. The Examiner's rejection seems to be on the basis that the exact verbiage of the claims is not recited in the specification.

Applicants vigorously differ with the Examiner that a specific example must be recited in the specification or that the exact verbiage of the claims must be recited in the specification in order to meet the written description requirement whereas all that the law requires is to provide adequate support for a claimed subject matter enough to find that the Applicant had possession of the claimed subject matter at the time of filing the application. Moreover, the Application

recited preferred modes which are 25 % or less allergenic activity of the derivative compared to the wild type allergen. Applicants even went further to recite the most preferred mode which is substantially no allergenic activity.

Applicants have canceled claims 35 and 36 merely to advance the prosecution of this application. Applicants are in no way conceding that blocking antibodies producing allergen derivative which elicit less than 10%, 5%, IgE binding to the wild type allergen are outside the scope of this invention. In particular, that limitation is embodied in properly construed claim 33. Most importantly, it is the object of the present invention to provide a method for treating or preventing allergic disorders by derivatizing wild type allergens and selecting those of them that elicit blocking anti-bodies that prevent IgE antibodies from binding to the respective wild type protein from which the derivative was derived. As such, consistent with the object and description of the present invention, a derivative that will elicit IgG antibodies that will totally eliminate IgE binding to wild-type allergens is most preferred. One of skill in the art understands that "substantially no allergenic activity" means that the IgE binding to the naturally occurring allergens is either totally eliminated or if present, is so present in an undetectable manner but in any case, does not elicit the symptomatologies connected with allergic reactions.

For at least the fact that there is no requirement to recite the exact verbiage of the claims in the specification, the Examiner is respectfully asked to reconsider the basis of this rejection and to withdraw it as improper.

Claim Rejections under 35 U.S.C. § 102(e)

Claims 33 – 40 and 43 – 48 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent Application Publication 2004/0091500 A1, (herein after referred to as the "alleged prior art"). The Examiner asserts that the claims of the present invention are not drawn to inducing blocking antibodies but to methods of treatment by administering an allergen derivative that either induces IgG antibodies or has decreased IgE binding as compared to

naturally occurring allergen. Applicants have amended the claims such that they are now directed to the administration of derivatives of naturally occurring allergen which induce blocking anti-bodies, said blocking antibodies, themselves acting to prevent or block the binding of IgE to naturally occurring allergens. Claim 33 has also been narrowed to recite the major allergens of alder, hazel and birch.

In order for the alleged prior art to form the basis of a 35 U.S.C. § 102 rejection, every element of the claimed invention must be identically shown in a single reference. In re Bond, 910 F.2d 831, 15 USPQ2d 156 (Fed. Cir. 1990). To that extent the prior art does not teach an allergy treatment based on use of derivatives that induce IgG production and reduce IgE binding and where such derivatives are selected from the major allergens of alder, hazel and birch. Accordingly, this ground for rejection should now be withdrawn.

Applicants hereby reiterate the remarks previously made in connection with this alleged prior art in the response to the first office action. Since the claims are now drawn specifically to a method of using derivatives isolated solely on the basis of their IgG induction capability and inhibition of IgE binding to wild type allergens, said method not in any way taught or suggested by the prior art, Applicants submit that this ground for rejection is now obviated and the rejection should be withdrawn.

The Examiner appears to be arguing that the administration of any reduced IgE binding derivative such as that of the prior art which might have the incidental effect of inducing IgG production anticipates the claims of the present invention. Applicants vigorously disagree on the grounds that the Examiner's contention is not grounded in the sciences of the invention. The Examiner, in effect is, contending that the IgE epitopic sites always coincide with the IgG epitopic sites.

As the Examiner is aware, formation of IgE antibodies against per se harmless antigens (i.e. allergens) is the hallmark and key pathomechanism of type I allergy. The methodology of the present invention is based on the theory that allergen-specific IgG antibodies, termed

blocking antibodies, can antagonize the cascade of allergic inflammation resulting from allergen recognition by IgE antibodies. The instant invention is based on the rationale that blocking antibodies inhibit allergen-induced release of inflammatory mediators from basophils and mast cells as well as IgE-facilitated allergen presentation to T cells, thus leading to suppression of T cell activation. Furthermore, the development of blocking antibodies is associated with reduced boosts of allergen-specific IgE production in patients receiving allergen-specific immunotherapy of the present invention. Thus blocking antibodies have protective activity by inhibiting immediate as well as late inflammatory responses and long-term ameliorating activity on the allergic immune response by antagonizing the underlying IgE production. Induction of blocking antibodies is thus an important mechanism underlying allergen-specific immunotherapy. See Specification pages 5 and 6.

As now distinctly claimed, a method of treatment using **derivatives** (not necessarily allergenic) capable of, **in vivo**, inducing IgG antibody production, while simultaneously inhibiting the binding of and or decreasing the production of allergen-specific IgE against naturally occurring allergens, are the derivatives of the present invention.

Contrastingly, the alleged prior art teaches **allergenic derivatives** characterized by reduced binding of IgE compared to the naturally occurring allergen as the recombinant allergens of the prior art. Specifically, paragraph 0030 of the alleged prior art teaches reduced binding of IgE by substitution of surface exposed amino acids while conserving α-carbon backbone tertiary structure. The methodology of the alleged prior art goes through an elaborate scheme of structural characterization of naturally occurring allergens followed by targeted amino acid substitution at B-cell eptitopic site such that the said tertiary backbone of the naturally occurring allergen is essentially preserved. Particularly, the structural elucidation of naturally occurring allergens is followed by targeted substitution at putative IgE binding sites such that the tertiary structure of the allergen is preserved.

The methodology of the instant invention is simple, elegant and very effective. It does not concern itself with structural characterization of the allergen, nor the experimentally intensive structural conservation of the allergenic derivative, but instead chooses such derivatives, of whatever structural configuration, derived by substitution, fragmentation or any other means in the art, that is capable of inducing sufficient IgG production in vivo, such that the binding of allergen-specific IgE to the naturally occurring allergen is substantially reduced, if not totally eliminated.

Thus, while the alleged prior art involves the concept of dominant IgE binding epitopes and the therapeutic concept of initiating a new protective immune response (see paragraph 0030), the instant invention is concerned with the induction of IgG as "protective antibodies", ie antibodies which possibly prevent IgE from binding to the respective wild type protein from which the derivative is derived. See page 4.

Roughly speaking, while the alleged prior art targets the epitopic specificity of IgE, the instant invention is concerned with the epitopic specificity of IgG, and the Applicants believe, teaches a highly effective method of treating allergic disorders not anticipated by the prior art.

Since the claims are now distinctly drawn to the use of derivatives that induce IgG production all the time, Applicants ask the Examiner to recognize that their method of treating allergic disorders is an elegant patentable departure from the experimentally intensive methodology of the alleged prior art. Applicants recognize that reduction or elimination of IgE binding is the ultimate therapeutic goal in the treatment of allergic disorders and that the complex patho-physiologic mechanisms of allergic response presents many therapeutic targets. Whereas the prior art taught IgE epitopic mapping and IgE epitopic manipulation of wild type allergens, it in no way concerned itself with IgG epitopic manipulation. The instant invention, on the other hand, and especially as now distinctly claimed, concerns itself with treatment using derivatives identified not laboriously by doing IgG epitopic mapping and manipulation, but simply

and quite elegantly, by identifying derivatives that elicit IgG production *in vivo*. This method of treatment is in no way taught by or anticipated by the prior art.

CONCLUSION

In view of the foregoing remarks, Applicants submit that there is no basis for applying the previous rejection to the pending claims and withdrawal of the rejections is respectfully requested. The claims are believed to be in condition for allowance, and Applicant earnestly solicits from the Examiner early notification of allowability.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, she is invited to contact the undersigned at his earliest convenience.

Respectfully submitted,

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